

We have to choose between a global market driven only by calculations of short-term profit, and one which has a human face.

Kofi Annan, address to World Economic Forum, 31 January 1999

WOMEN'S HEALTH

Does City Life Alter Breast Density?

Epidemiologic studies have found differences between urban and rural women in breast cancer incidence and mortality, both generally being higher in urban areas. Now a British study suggests that women who live or work in urban areas have denser breasts and thus potentially a greater risk of breast cancer, according to a report published online 19 December 2007 ahead of print in *Current Medical Research and Opinion*. The new findings add to the evidence that breast cancer risk is higher in urban settings and may eventuate in new breast cancer screening guidelines.

Breasts are made up of glandular and fatty tissue. Glandular tissue is denser than fatty tissue and harder to read on a mammogram; a higher percentage of dense tissue is also linked with increased risk of breast cancer. A meta-analysis of more than 40 studies published in the June 2006 issue of *Cancer Epidemiology, Biomarkers & Prevention* concluded that women with high breast density have a nearly 5-fold higher breast cancer risk than women with the lowest breast density.

The researchers analyzed digital mammograms of 972 women, including 318 women from London and 654 women from outside the capital. All the women had received mammography at The Princess Grace Hospital in London. The researchers found that women aged 45–54 who lived in central London were twice as likely to have very dense breasts as women who lived in outlying suburban and rural areas. Age-specific analyses indicated that breast density differences by area were more pronounced in women under age 50.

Study leader Nicholas M. Perry, director of the London Breast Institute at The Princess Grace Hospital, was not particularly surprised by the study's findings. While working as a radiologist over a 15-year period, Perry had observed that London women tended to have denser breasts than women living in outlying areas. These personal observations were the main impetus for the study. "Our study was not designed to do anything other than report on the original observation that urban women seemed to have denser breasts," he says. "Since releasing our findings, I have received numerous comments from radiologists who have observed the same phenomenon."

The biological basis for the new finding remains to be determined. "It may simply be that London women are thinner than women living outside the capital, or it may be due to other factors," says coauthor Stephen Duffy, an epidemiologist at Cancer

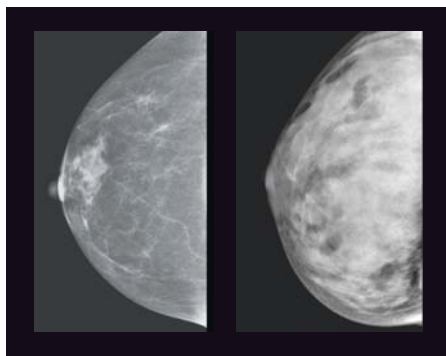
Research UK and Queen Mary, University of London. "We need to carry out research on density and other breast cancer risk factors at the individual level by area of residence to get to the bottom of this."

Although mammographic density is a strong risk factor for breast cancer, it is not the only one. As an observational study, the London study did not control for factors such as suboptimal body weight, which also can influence density and is an independent risk factor for breast cancer.

"Before it can be concluded that urban or rural residence influences mammographic density, it must be shown that the individuals living in urban or rural environments do not differ in one or more factors that influence density," says Norman Boyd, a senior scientist at the Campbell Family Institute for Breast Cancer Research at Princess Margaret Hospital in Toronto. "Body weight is a strong influence on density, and it is known that obesity is more common in rural than in urban settings, and that obesity is less common among professionals than in those with other occupations. Both of these factors could explain the observed findings. If those in rural settings also had more children, that could also contribute." Boyd's research team is presently focused on identifying the genetic and environmental factors that influence mammographic density and the relationship of these factors to breast cancer risk.

Perry's team speculates that their observations can be at least partially attributed to environmental factors such as estrogenic particles present in traffic emissions. They present this argument in a letter to the editor published online 8 December 2007 ahead of print in *Cancer Causes & Control*. Still, Perry cautions that more research is needed to determine the underlying reasons for this phenomenon, taking into account stress as well as lifestyle and environmental factors. "We intend to carry on with this research in the form of an intervention trial and hope other groups will do the same," he says. "There is also likely to be a consensus conference before long addressing the issue of breast density and how it is modulated."

In the interim, he urges urban women to be especially vigilant about breast cancer screening and to rely primarily on digital mammography, which is more effective than conventional mammography at detecting cancer in dense breast tissue. At the present time, only about 25% of centers in the United States and 10% of mammography centers in England offer digital mammography. —M. Nathaniel Mead



Population density? Observational data suggest city women have denser breast tissue than women in outlying areas, but the reason for the difference is unclear (inset, l-r: less dense and more dense breast tissue).

Alex Nikada/Stockphoto; insets: Radiological Society of North America

INNOVATIVE TECHNOLOGIES

Transportation Fuels on the Table

On 29–30 November 2007, just days before the United Nations Climate Change Conference began in Bali and Al Gore and Rajendra Pachauri received the 2007 Nobel Peace Prize for their work on climate change, the U.S. Institute of Medicine (IOM) held a workshop to highlight gaps in scientific understanding about the environmental and human health effects of transportation fuels. The transportation sector's use of fuel is expected to grow more quickly than demand for energy in any other sector between 2005 and 2030, Scott Nauman, manager of economy and energy in the ExxonMobil Corporate Planning Department, told conference attendees. Therefore, new transportation fuels are key players among the innovative technologies being investigated and developed to help countries throughout the world cut greenhouse gas emissions.

As worldwide transportation fuel use rises, the emissions and carbon dioxide emitted by burning these fuels will also rise, pointed out Samuel Wilson, acting director of the NIEHS. "We want to add 'minimizing the human health impact' . . . to the criteria for developing alternative fuels," he said.

According to Michael Wang, a vehicle and fuel systems analyst at the U.S. Department of Energy Argonne National Laboratory, biofuels are considered the most promising alternative for reducing petroleum use and decreasing greenhouse gas emissions from transportation. Electricity is also expected to grow as a source for plug-in hybrids, as is hydrogen. The idea of producing transportation fuels from coals "has generated some interest lately because they can be produced domestically," Wang says, but their carbon emissions are "pretty high."

The main biofuel currently being developed for transportation in the United States is ethanol from corn via distillation, and its production is increasing rapidly. According to the Energy Information Administration, the percentage of the U.S. gasoline pool represented by ethanol rose from 1.27% in

2000 to 2.85% in 2005. However, John Regalbuto, director of the National Science Foundation's Catalysis and Biocatalysis Program, predicts that hydrocarbon-based "green gasoline," "green diesel," and "green jet fuel" will represent a significant fraction of new biofuels by 2022. When produced via catalysis from materials such as switchgrass and waste wood products, the performance of these renewable biofuels are "essentially the same" as their conventional counterparts, he says. However, their manufacture involves intermediates such as hydroxymethylfurfural and ionic liquid solvents that require further study in terms of health effects.

Additives also affect the emissions of transportation fuels, as well as these fuels' impact on the environment, stressed Serap Erdal, an assistant professor at the University of Illinois–Chicago School of Public Health. Uncertainty over which addi-

tives will be added to new fuels and how the complex mixtures will behave in the environment makes it very hard to predict potential health effects, agreed the experts amassed at the IOM meeting. In the United States, for example, ethanol has only recently been used as an additive to make gasoline burn more efficiently. But in Brazil, where ethanol has been used as a fuel for nearly 30 years, it has become clear that, compared with gasoline, the sugarcane-derived fuel produces much higher emissions of formaldehyde, a known human carcinogen, and acetaldehyde, a suspected human carcinogen, said Paolo Saldiva, a professor of medicine in the University of São Paulo's Department of Pathology. However, he said that the health effects of exposure to these compounds via air emissions are unclear.

What is indisputable is that key decisions leading to the development of new fuels will be made before the requisite health effects data are available, so "we need to get going as soon as possible . . . to collect baseline data," said Dan Greenbaum, president of the Health Effects Institute, which published a report summarizing the health effects of exposure to 21 mobile source air toxics in November 2007. Added Erdal, "There is a critical need to institute public health surveillance so that we are already collecting data and are able to detect changes as they take place." —**Kellyn S. Betts**



Antibacterial Alters Hormone Activity

In a study published online 29 November 2007 ahead of print in *Endocrinology*, researchers at the University of California, Davis, report that the commonly used antibacterial chemical triclocarban (TCC) acts as an endocrine disruptor by a previously unreported mechanism. In human cells, the researchers found that TCC increased gene expression that is normally regulated by testosterone. In male rats, they found that testosterone-dependent organs grew abnormally large after the rats were fed TCC. Until this study, endocrine disruptors had only been found to block the effects of hormones. TCC has been used in a variety of household and personal care products for more than 45 years.



Raising Awareness of Nurse Health

On 11 December 2007, the Environmental Working Group released the results of a survey of occupational health among nurses. More than 1,500 U.S. nurses participated in the online survey, which assessed workplace exposures to common hazardous substances and other agents as well as the health of nurses' children. As had been seen in earlier studies, nurses who experienced routine high exposures to sterilizing and cleaning chemicals, residues from drug preparation, anesthetic gases, radiation, and other hazardous agents reported higher rates of asthma, miscarriage, and certain cancers, and their children had higher rates of cancer and birth defects (especially musculoskeletal defects). The goal of the survey was to encourage hospitals to minimize risks to nurses and inspire further study.

Minnesota Bans Mercury in Beauty Products

On 1 January 2008, Minnesota became the first state to ban mercury from cosmetics such as mascara, eyeliner, and skin-lightening creams. Current federal regulations allow up to 65 ppm mercury to be used in cosmetics as a preservative and germicide. The cosmetics industry claims the levels of mercury found in cosmetics pose little risk to human health, but an August 2005 WHO policy paper asserts that "studies suggest that mercury may have no threshold below which some adverse health effects do not occur." Skin-lightening creams could pose more of a health risk as people generally apply relatively large amounts of them over sizeable areas of their bodies.



CANCER

Stress Link Redefined

As the battle against cancer continues, doctors, researchers, and patients continue to investigate new avenues for prevention and treatment. But the struggle isn't getting any simpler. Researchers in a handful of laboratories have recently documented that, among many other triggers and promoters, stress hormones are a direct contributing factor in the progression of ovarian and nasopharyngeal cancer. Now a team from The Ohio State University has discovered a similar link with a third cancer, multiple myeloma.

Multiple myeloma, which involves lymphoid tumors, kills more than 10,000 Americans annually, usually within 3 to 4 years of diagnosis. Ovarian and nasopharyngeal cancers are characterized by solid epithelial tumors and result in about 15,000 and 650 U.S. deaths per year, respectively.

Until recently, stress hormones were thought to simply weaken the immune system and impair the body's ability to fight cancer. Instead, the new evidence is showing that stress hormones such as norepinephrine, epinephrine, and cortisol, whether induced by psychological stimuli or environmental agents such as cold temperatures or infectious diseases, may play a much different role in cancer progression than generally presumed.

The Ohio State researchers began their study, published online 5 November 2007 ahead of print in *Brain, Behavior, and Immunity*, with a few givens: multiple myeloma has been linked with increased growth of supporting blood vessels, and vascular endothelial growth factor (VEGF) has been shown to play a role in that vessel growth. The team evaluated 3 human cell lines from 3 patients, representing different stages of multiple myeloma, to see if either of 2 doses of norepinephrine played a role in the expression of VEGF in the cell lines.

Based on their assessment of selected adrenergic receptors in the cell lines, they found that norepinephrine stimulated all 3 cell lines. The FLAM-76 cell line taken from bone marrow, which represented the earliest stage of multiple myeloma, showed the most significant stimulation.

Responses in all 3 cell lines were dose- and time-dependent, but there were no distinct patterns. Depending on the circumstances, either the higher or lower dose induced the most stimulation or suppression, and there were large differences over 1-, 3-, 6-, and 24-hour periods.

Eric Yang, lead author of the study and a research scientist at The Ohio State University Institute for Behavioral Medicine Research, points out that the effect on multiple myeloma of chronic stress from single or multiple sources is unknown. In addition, he says that the lowest concentration of norepinephrine tested was 10 times higher than levels typically detected in stressed humans. However, he says the team's attempts to test at more realistic concentrations were stymied by erratic results that were difficult to interpret. But analogous research on ovarian cancer has shown similar effects at realistic doses.

Anil Sood, a professor of gynecologic oncology and cancer biology at the University of Texas M.D. Anderson Cancer Center, says that for stress and cancer the effects of other variables such as age, sex, race, ethnicity, and genetic makeup also remain a puzzle, and that there is little information on how best to manage or treat chronic stress in order to reduce its potential effects on tumor growth. Another concern is that the cell lines were grown in a tissue culture that can't represent what actually occurs in the body, says Bruce Rabin, a professor of pathology, psychiatry, and psychology at the University of Pittsburgh School of Medicine. However, Rabin says the evidence from the experiments is a good first indication of possible effects of stress hormones on multiple myeloma. —**Bob Weinhold**

GENETIC RESEARCH

Selfish DNA versus Vector-Borne Disease

Malaria, carried by *Anopheles* mosquitoes, infects up to 500 million people each year and kills 1 million, most of them children in sub-Saharan Africa. Dengue fever, a viral disease transmitted by *Aedes* mosquitoes, is now endemic in more than 100 countries and strikes an estimated 50 million people per year. Major international efforts to control, prevent, or eradicate these diseases are in place, but traditional methods such as vaccines and insecticides have met with limited success. Now scientists are exploring the use of so-called selfish DNA to bioengineer mosquitoes that will take over vector populations, eventually suppressing the diseases altogether.

Selfish DNA is defined as a segment of the genome with no apparent function other than to ensure its own replication. Such elements—which include transposons and homing endonuclease genes—are unique in

that they can replicate themselves within a genome and are not necessary for the reproductive success (or “fitness,” in evolutionary terms) of the host organism. Selfish genes may be the ideal vehicles to deliver knockout blows to vector-borne diseases.

“You can do this in two ways,” says Fred Gould, a professor of entomology at North Carolina State University. “One is to have the selfish DNA element be neutral—that is, it just inserts itself into the population and doesn't actually lower the fitness of the organism, but it carries with it . . . an antipathogen gene. So you wind up with a population that looks the same and has the same fitness, but can't transmit the disease. The other approach is to actually have these selfish genes drive through a [vector] population and decrease its fitness, so that their density goes down.”

Some of these methods have shown success in the laboratory, but they are all still many years away from field deployment. Hoping to accelerate that process, Gould and 2 colleagues organized a conference held 5–7 December 2007 at the National Evolutionary Synthesis Center (NESCent) in Durham, North Carolina. Part of



Mosquito larvae to be tested for malaria, Kenya

NESCent's mission is to host “catalysis meetings”—intensive interactive sessions that bring together diverse groups to spark

ehpnet

Consumer Action Guide to Toxic Chemicals in Toys

On 5 December 2007, the nonprofit Ecology Center launched the Consumer Action Guide to Toxic Chemicals in Toys at <http://www.healthytoys.org/> to provide parents and other caregivers with information on toys containing potentially hazardous chemicals such as lead, arsenic, and mercury. The site currently contains basic screening information on more than 1,200 toys that were tested using X-ray fluorescence to determine amount of various chemicals on a toy's surface. Each toy receives an overall rating as well as separate ratings for 5 chemicals—lead, chromium, chlorine/PVC, arsenic, and mercury. The ratings are not intended to measure health risk or actual user exposure.

The Product Action Guide lists toys by manufacturer and type and by best and worst rated; visitors can also search by specific toy name. Each toy's page lists its ratings as well as an overview of which parts of the toy were tested, and the amounts of the chemicals of concern detected. Also noted is the presence of other potentially toxic chemicals such as tin, antimony, chromium, and bromine if levels above 100 ppm were found (these chemicals are not, however, used in calculating the overall rating for items).

The Buy Toys Safely page under the Take Action subhead offers advice for buying safer toys. The site also has a list of frequently asked questions that includes topics ranging from lead paint in homes to how to find out about product recalls. In the Chemicals of Concern section, visitors can learn about the chemicals tested, alternatives to these chemicals, and other resources for information on healthy products, toy safety, and ecolabeling programs in the United States and abroad. Visitors can also use the Test My Toy! feature to nominate additional toys for testing. In the site's first 2 weeks, more than 4,500 additional toys were nominated, of which 22 were tested. —Erin E. Dooley

new ideas and new collaborations in emerging fields.

"Selfish DNA and the Genetic Control of Vector-Borne Diseases" gathered approximately 30 researchers whose work ranges from basic to applied science, and whose focus ranges from the molecular to the population level. "Having people with really specific expertise in the basic sciences talking to people who are trying to apply these things gave good insights," says Gould. "There was a deep interdisciplinary interaction, and it wasn't just superficial or lip service."

Participants discussed some of the enormous challenges that remain to be overcome before any of these strategies will be ready for large-scale deployment. Among these are perfecting the models and determining the optimal combination of gene drive systems (i.e., methods of effectively introducing the desired gene into the population) and effector genes (which encode the antipathogenic element) to maximize vector control and minimize the development of resistance by the pathogens.

So when might we realistically expect to see mosquitoes modified with selfish DNA deployed in the field? "We've been saying ten years for the last ten years," says Anthony

James, a professor of microbiology and molecular genetics at the University of California, Irvine, and principal investigator for a large, multicenter research project into several of the applications being developed for genetic control of dengue virus transmission. "It's such an adjustable horizon because as we get closer to something actually working, the size and scope of the challenges actually change." The risk, says Gould, is that a prematurely deployed system would fail to control the disease, resulting in a rebound effect by resistant disease strains and perhaps permanently closing the window on all genetic control strategies.

Another question is whether the public can—or indeed should—accept the idea of releasing genetically modified organisms into the environment, let alone insects that are encouraged to spread, invade, and supersede native populations. Says Gould, "I think it's important to stress that there are a million children a year dying of malaria, and preventing that is a much bigger benefit than the risk of a single gene moving into another *Anopheles* species—the risks of genes moving and disrupting habitats are small."

—Ernie Hood

Hops for Health?

Xanthohumol, a flavonoid compound found in the hop plant, is a powerful antioxidant that can reduce the activity of cancer-causing cytochrome P450 enzymes. Earlier studies have found that xanthohumol can kill cultured breast, colon, ovarian, and prostate cancer cells, and can also reduce the oxidation of LDL ("bad") cholesterol. Now an article in the November 2007 issue of *Apoptosis* shows that xanthohumol induces apoptosis in adipocytes and inhibits adipogenesis in maturing preadipocytes, leading its authors to conclude the compound could be useful as an antiobesity agent. Also in autumn 2007, the German company TA-XAN AG launched XAN Wellness, the first product to employ a patented process that supposedly boosts the health-promoting properties of xanthohumol.



New Tactic for Taming Invasive Species

Each year, in response to rules adopted in 2004 by the International Maritime Organisation (IMO), the shipping industry spends billions of dollars to remove exotic species from the 3–5 billion tons of water transported in ballast tanks. A South African company, Resource Ballast Technologies, is on track to commercialize a new system for this purpose that, unlike some conventional methods, does not use harmful chemicals. Instead, it combines ozone and ultrasonic radiation to kill organisms. The small unit fits on existing ballast discharge pipes. The company has submitted its technology to the IMO for approval.

Germany Takes Aim at Auto Emissions

On 1 January 2008, the German cities of Berlin, Cologne, and Hanover witnessed the rollout of a new program to reduce air pollution in city centers. In those cities, and in 17

more to be added during the year, cars are required to display color-coded stickers that reflect how much fine particulate pollution they emit, as determined by an authorized testing facility. Cars that emit too much particulate matter will not be allowed in central "environmental zones,"

or *umweltzones*, of participating cities. Drivers who enter city centers without a sticker will receive a fine of up to US\$60 dollars and a point on their driver's license. The new laws are part of an effort to help Germany meet new European Union standards for air quality.

